

## **Neonatal Abstinence Syndrome: Indian Health Service (IHS) Best Practices Guidelines**

### **1. Neonatal Drug Withdrawal**

Intrauterine exposure to certain drugs and medications can cause clinical symptoms in the newborn after delivery. Symptoms in infants can be caused by chronic exposure, toxicity, or withdrawal from the substance. Clinically significant symptoms of withdrawal are most commonly seen after exposure to tobacco, SSRIs, and opioids, but can also be seen in infants exposed to benzodiazepines, barbiturates and alcohol. Polydrug exposure is common and can exacerbate symptoms of withdrawal. Timing of onset of neonatal drug withdrawal and signs and symptoms of withdrawal depend on the medication or drug that was used during pregnancy. (See Table 2)

### **2. What is Neonatal Abstinence Syndrome (NAS)?**

Neonatal Abstinence Syndrome (NAS) refers specifically to neonatal withdrawal from opioids. Common opioids that can lead to NAS include short acting opioids including hydromorphone, oxycodone, morphine, and heroin, and long acting opioids including methadone and buprenorphine. NAS describes a constellation of symptoms including CNS irritability, autonomic instability, and GI dysfunction. NAS occurs in 55-94% of infants exposed to opiates and varies in severity from mild to life-threatening. Clinical signs and symptoms of NAS depend on multiple factors including the type of opioid the infant was exposed to, timing of exposure before delivery, maternal health, and maternal and infant metabolism.

### **3. Identification of infants at risk for Neonatal Drug Withdrawal**

Infants at risk for withdrawal can be identified by maternal past medical history and pregnancy history, maternal urine drug screen, infant urine and meconium drug screen, or umbilical cord drug screen. Screening for substance use both licit and illicit should begin early in pregnancy. Risk factors for NAS in the maternal history include known history of opioid use or abuse in current pregnancy or a known history of use of abuse, use of prescription medications for pain control, late or no prenatal care, or unexpected complications of pregnancy known to be associated with drug use including unexplained late fetal demise, precipitous labor, placental abruption, preterm labor, PROM, or history of repeated spontaneous abortions. Maternal behaviors that are concerning for intoxication or drug use or unusual erratic behavior should be considered risk factors for NAS. Signs or symptoms in the infant that suggest NAS can also identify infants at risk for NAS.

All infants exposed to opioids during pregnancy, including opioids prescribed by a physician, should be monitored for NAS after delivery. The risk of an infant developing NAS may be lower if the mother has not used opiates for 14 days prior to the birth, although NAS still can occur even when opioids are used in the first trimester without history of ongoing use in second and third trimesters. Depending on the method used for testing, and the dose taken, the urine drug screen picks up

usage of short acting opioid use up to about 72 hours after last use, and long acting opioid use (such as methadone or buprenorphine) up to 5 to 7 days after last dose. In some locations buprenorphine tests have to be ordered separately from other urine drug screening panels. The desired tests should show positive for methadone or buprenorphine if the woman is on medication assisted treatment/maintenance. Note: medication assisted treatment is standard of care and discontinuation of opiate use in pregnancy can be dangerous to the fetus and thus is not routinely recommended. Opioid detoxification during any phase of pregnancy is contraindicated due to the high risk of spontaneous abortion resulting from the traumatic physiological stress of opioid withdrawal to the pregnant mother and developing fetus.

Women identified as using illicit opioids during pregnancy should be transitioned to maintenance therapy. Medication assisted treatment is standard of care and discontinuation of opiates during pregnancy can lead to fetal distress and miscarriage.

“Maintenance therapy with methadone or buprenorphine is the standard treatment of opiate addiction during pregnancy. The rationale for opioid-assisted therapy during pregnancy is to prevent complications of illicit opioid use and narcotic withdrawal, encourage prenatal care and drug treatment, reduce criminal activity, and avoid risks to the patient of associating with a drug culture. Medically supervised withdrawal from opioids in opioid-dependent women is not recommended during pregnancy because the withdrawal is associated with high relapse rates. However, if methadone maintenance is unavailable or if women refuse to undergo methadone or buprenorphine maintenance, medically supervised withdrawal should ideally be undertaken during the second trimester and under the supervision of a physician experienced in perinatal addiction treatment (13). If the alternative to medically supervised withdrawal is continued illicit drug use, then a medically supervised withdrawal in the first trimester is preferable to waiting until the second trimester.” (Committee on Health Care for Underserved Women and the American Society of Addiction Medicine. Opioid Abuse, Dependence, and Addiction in Pregnancy. ACOG Policy Statement Number 524 May 2012.)

#### **4. Delivery Room Management of Infants at Risk for NAS**

**Efforts should be made by the delivering physician to adequately address maternal pain control during labor and delivery.**

**For infants exposed to opioids prenatally the use of Naloxone is contraindicated in the delivery room.**

#### **5. Care of infants at risk for NAS**

In accordance with its system wide adoption of the Baby-Friendly Hospital Initiative, the Indian Health Service recommends that all infants are cared for using the principles of rooming in and close mother/infant contact whenever safe. Breastfeeding, skin to skin care, swaddling, and rooming in have been associated with decreased severity of NAS.(2, 3) Skin to skin care and swaddling can help to reduce uninhibited gross motor dysregulation.

Infants at risk for NAS should be screened at the time of delivery with urine, meconium or umbilical cord drug screening. Basic interventions should not be delayed pending the results of screening. Risk of NAS is not a contraindication to breastfeeding and breastfeeding should not be delayed pending the results of drug screening.

## 6. Assessment for Signs and Symptoms of NAS

Infants at risk for NAS should be monitored in the hospital for signs and symptoms of withdrawal. Due to the location of the opioid receptors in the brain and gastrointestinal tract, signs and symptoms of NAS can be categorized as neurological, gastrointestinal and autonomic. (see table 2). A semi-objective assessment of these signs and symptoms is facilitated by using a scoring tool to help monitor infant for NAS. Several scoring tools exist including the Lipsitz tool and Finnegan scoring tool. The most commonly used scoring tool is the Modified Finnegan Scoring Tool. Scoring should begin between 2 and 4 hours of life and continue every 4 hours for the duration of the observation period. Parents should be educated about the scoring tool being used and invited to participate in scoring to the greatest extent possible. When using the Finnegan scoring tool two consecutive scores greater than 12 or three consecutive scores greater than 8 indicate a need for treatment with medications.

Infants exposed to short acting opiates should be observed in the hospital for a minimum of 72 hours. Infants exposed to longer acting maintenance opioids including methadone and buprenorphine should be observed for a minimum of 5 days. Withdrawal from long acting opiates can begin as long as 2 weeks after delivery and parents should be educated about signs and symptoms of NAS that may require medical care prior to discharge from the hospital or birthing center.

## 7. Clinical Signs of Withdrawal (1)

Table 1: Withdrawal Signs and Symptoms

Neurological	Gastrointestinal	Autonomic
<ul style="list-style-type: none"> <li>• Irritability</li> <li>• Increased wakefulness</li> <li>• High-pitched cry</li> <li>• Tremor</li> <li>• Increased muscle tone</li> <li>• Hyperactive deep tendon reflexes</li> <li>• Frequent yawning</li> <li>• Sneezing</li> <li>• Seizures</li> </ul>	<ul style="list-style-type: none"> <li>• Vomiting</li> <li>• Diarrhea</li> <li>• Dehydration</li> <li>• Poor weight gain</li> <li>• Poor feeding</li> <li>• Uncoordinated and constant sucking</li> </ul>	<ul style="list-style-type: none"> <li>• Diaphoresis</li> <li>• Nasal stuffiness</li> <li>• Fever</li> <li>• Mottling</li> <li>• Temperature instability</li> <li>• Mild elevations in respiratory rate and blood pressure</li> </ul>

## 8. Onset of Withdrawal Symptoms

Onset of withdrawal depends on the half-life of the drug, duration of the addiction, and time of last maternal dose prior to delivery.

Table 2: Estimated Withdrawal Onset

<b>Drug</b>	<b>Approximate time to onset of withdrawal symptoms</b>
Barbiturates	4-7 days but can range from 1-14 days
Cocaine	Usually no withdrawal signs but sometimes neurobehavioral abnormalities (decreased arousal and physiologic stress) occur at 48-60 hours and dysregulation can potentially last for several months.
Alcohol	3-12 hours
Heroin	Within 24 hours
Marijuana	Usually no clinical withdrawal signs but dysregulation may be long-acting
Methadone	3 days but up to 5-7 days; rate of severity of withdraw cannot be correlated to dose of maternal methadone
Methamphetamines	Usually no withdrawal signs but sometimes neurobehavioral abnormalities (decreased arousal, increased physiologic stress, and poor quality of movement) occur at 48-60 hours and dysregulation can potentially last for several months.
Opioids	
<b>Short term acting</b>	1-3 days
<b>Long term acting</b>	2-6 days
Sedatives	1-3 days
SSRIs	Several hours to several days—withdrawal linked with third trimester use

These symptoms are likely seen after exposure to buprenorphine (Subutex/Suboxone), codeine, heroin, hydrocodone (Lortab, Vicodin), hydromorphone (Dilaudid), methadone, morphine, oxycodone (Percocet). Opioid withdrawal syndromes can persist from days to months depending on the half-life of the agent and pharmacokinetics. Polysubstance-dependency is likely seen with the above drugs as well as barbiturates, sedatives, SSRIs.

## 9. Non-Pharmacologic Interventions

**All infants at risk for NAS should be cared for with non-pharmacologic interventions starting at the time of birth. The goal of non-pharmacologic interventions, or supportive care, is to create a calm quiet and controlled environment where there is minimal stimulation for the newborn.**

Non pharmacologic methods include:

- Swaddling
- Skin to skin with parent
- Rocking
- Rooming in
- Minimal sensory or environmental stimulation
- Maintain temperature stability
- Providing baby with a pacifier for non-nutritive sucking
- Breast milk feedings when appropriate can help reduce the need for pharmacological intervention
- Feeding (consider alternating breast/bottle and pacifier during feed to compensate for excessive sucking and possibly prevent emesis)

## **10. Nursing care of infant on NAS treatment**

Pharmacological treatment will be started dependent on a safe staffing ratio. The American Academy of Pediatric Guidelines for Perinatal Care (1997) suggest a minimum staffing of one registered nurse for every two to three patients in intermediate care and one nurse for every one to two patients in intensive neonatal care. Cardio-respiratory monitoring is required for all infants started on morphine and will need to be continued for 4 days and/or until the dose is reduced. Further monitoring should then be at the discretion of the physician. If infants reach the threshold for pharmacological treatment and treatment cannot be started due to unsafe staffing ratios, infants should be transferred to a hospital that can provide them with the pharmacological treatment required.

## **11. Pharmacologic Therapies**

**Clinical signs and symptoms of NAS that interfere with the infant's ability to have adequate growth and social interaction may be an indication for pharmacologic therapy. When using the Finnegan scoring tool this is generally considered to be two consecutive scores greater than 12 or three consecutive scores greater than 8. Currently, there is no universally recommended dosing or weaning regimen for treating NAS.**

***Note : Dose is in mg/kg; NOT in absolute milligram dosing***

Begin when 3 consecutive Finnegan scores are > 8 or when the sum of 3 consecutive Finnegan scores is > 24.

Use morphine as the first-line agent and the mainstay of treatment.

0.04 mg/kg PO is recommended starting dose for NAS. Increase dose to 0.08mg/kg PO q4 hours if Finnegan scores remain >8. Maximum dose is 0.2mg/kg PO q4 hours.

## 12. Weaning from Medication

After a 48 hour period of stabilization, the infant may be gradually weaned from medication. Morphine can be weaned by 0.02 mg every 24 hours as long as NAS scores remain <8. The weaning process is deferred for one score >8. If the infant has a score >8, he should be rescored in one hour. If the infant has 2 NAS scores >8, treatment must be re-escalated. ***Some infants have a biphasic course of NAS, with two rather than one peak NAS severity.*** In general, reescalation doses are half of the initial doses, as increased NAS severity after an initial period of stabilization is generally of reduced symptom intensity. To re-escalate treatment, increase morphine by 0.01 mg every 3 - 4 hours for 2 scores >8. For two scores >12, increase morphine 0.02 mg every 3-4 hours. A plateau of scores below 9 for 48 hours is required for re-weaning, which occurs as above.(4) Patients who have had pharmacologic treatment discontinued should be monitored a minimum of 24-48 hours prior to discharge for rebound symptoms. Weaning should always be done according to protocol. Evidence suggests that while no specific weaning protocol is optimal, the act of weaning according to a protocol results in fewer days of opioid treatment and shorter length of stay. (Hall et al. **A Multicenter Cohort Study of Treatments and Hospital Outcomes in Neonatal Abstinence Syndrome. 2014 Pediatrics 134(2) e527-e534**) The recommended length of stay for withdrawal from a short acting opioid is 3 days and long acting opioids require 5 days or longer according to the American Academy of Pediatrics guidelines.

## 13. Breastfeeding:

*The Academy of Breastfeeding Medicine Protocol Committee. ABM Clinical Protocol #21: Guidelines for Breastfeeding and the Drug Dependent Woman. Breastfeeding Medicine 2009 4(4) 225-228):*

Please note that the following recommendations are based largely on expert opinion because of the sparse research base on these issues.

Women who meet all of the following criteria under the following circumstances should be supported in their decision to breastfeed their infants:

- Women engaged in substance abuse treatment who have provided their consent to discuss progress in treatment and plans for postpartum treatment with substance abuse treatment counselor
- Women whose counselors endorse that she has been able to achieve and maintain sobriety prenatally; counselor approves of client's plan for breastfeeding
- Women who plan to continue in substance abuse treatment in the postpartum period
- Women who have been abstinent from illicit drug use or licit drug abuse for 90 days

prior to delivery and have demonstrated the ability to maintain sobriety in an outpatient setting

- Women who have a negative maternal urine toxicology testing at delivery except for prescribed medications
- Women who received consistent prenatal care
- Women who do not have medical contraindication to breastfeeding (such as HIV)
- Women who are not taking a psychiatric medication that is contraindicated during lactation
- Stable methadone-maintained women wishing to breastfeed should be encouraged to do so regardless of maternal methadone dose.
- Women under the following circumstances should be discouraged from breastfeeding:
  - Women who did not receive prenatal care
  - Women who relapsed into illicit drug use or licit substance misuse in the 30-day period prior to delivery
  - Women who are not willing to engage in substance abuse treatment or who are engaged in treatment but are not willing to provide consent for contact with the counselor
  - Women with positive maternal urine toxicology testing for drugs of abuse or misuse of licit drugs at delivery
  - Women who do not have confirmed plans for postpartum substance abuse treatment or pediatric care
  - Women who demonstrate behavioral qualities or other indicators of active drug use
- Women under the following circumstances should be carefully evaluated, and a recommendation for suitability or lack of suitability for breastfeeding should be determined by coordinated care plans among perinatal providers and substance abuse treatment providers:
  - Women relapsing to illicit substance use or licit substance misuse in the 90–30-day period prior to delivery, but who maintained abstinence within the 30 days prior to delivery
  - Women with concomitant use of other prescription (i.e., psychotropic) medications
  - Women who engaged in prenatal care and/or substance abuse treatment during or after the second trimester
  - Women who attained sobriety only in an inpatient setting

While maternal prescription opioid use and buprenorphine maintenance may be safe for infants of some lactating women, the research literature is too sparse for recommendations to be made about these substances.

**Breast milk intake is associated with reduced neonatal abstinence syndrome severity, delayed onset of neonatal abstinence syndrome, and decreased need for pharmacologic treatment, regardless of the gestation and the type of drug exposure.** (Abdel-Latif et al. Effects of Breast Milk on the Severity and Outcomes of Neonatal Abstinence Syndrome Among Infants of Drug Dependent Mothers. Pediatrics 2006; 117:e1163)

Many nurseries around the country are also using formula supplementation right now although there is no strong evidence for doing this. Most nurseries are using low lactose formula (sensitive or similar) and some nurseries are even using 22 calorie formulas. **Babies who are withdrawing can have significantly elevated calorie needs up to 150 kcal/kg/day.**

## References

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